REMARKS

Applicant respectfully requests entry of the remarks submitted herein. No claims were amended. Applicant thanks the Examiner for the telephone conferences of February 10, 2004 and February 12, 2004. Reconsideration of the pending application is respectfully requested.

The 35 U.S.C. §103 Rejections

Claims 1, 4, 7-9, 27, and 31 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Sugitachi et al., Fischer et al. or DE 3007226 taken with WO 92/14480 and Poelstra et al. and further in view of Millan et al. This rejection is respectfully traversed.

In the January 21, 2004 Advisory Action, the Examiner stated that this rejection was maintained because the claims only require that "the composition be applied topically," which, according to the Examiner, is how the individual components disclosed in the cited references are applied. Contrary to the Examiner's statement, the claims do not only require that "the composition be applied topically." In addition to claim 1 requiring that the composition be "formulated for topical delivery," claim 1 also requires that the composition includes placental alkaline phosphatase and a gel forming material, and further requires that the placental alkaline phosphatase is present in the composition "in an amount effective for stimulating proliferation of fibroblasts...."

The Sugitachi et al. reference, the Fischer et al. reference, the DE 3007226 reference, and the WO 92/14480 reference teach that a number of compounds can be used for wound healing and that such compounds can be incorporated into a gel material. In particular, the Sugitachi et al. reference discloses that Factor XIII, with or without thrombin, can be attached to a structure such as a gelatin sponge and applied to a wound site. The Fischer et al. reference discloses a bandage composition that, in addition to components such as antiseptics, antibiotics, medicinal substances, nutrients, hormones, and local anesthetics, can contain a gel or agarose component. The DE 3007226 reference discloses that chlorhexidine and allantoin can be incorporated into gelatin capsules and can exert a synergistic effect on wound healing. The WO 92/14480 reference discloses administering recombinant G-CSF or GM-CSF to a wound to accelerate healing. None of these references mention alkaline phosphatase, let alone placental alkaline phosphatase.

With respect to the Poelstra et al. reference, the Examiner specifically pointed to column 4, line 53 in the telephone conference of February 12, 2004, to support the obviousness rejection. The paragraph at column 4 in the Poelstra et al. reference generally discloses that alkaline phosphatase can be involved in promoting calcification of bone (column 4, line 15), promoting mineralization of bone (column 4, line 27), and improving osteogenesis (column 4, line 42). The specific section of the Poelstra et al. reference that includes line 53 discloses that:

> "[a] derivative of alkaline phosphatase with fibrillar collagen is not suitable for systemic application as fibrillar collagen induces intravascular platelet activation leading to embolisms. Therefore, a complex of fibrillar collagen and alkaline phosphatase could not be used in a method for treating osteoporosis or osteomalacia or any other bone defect which requires systemic application. It can only be used when immobilized in situ at the location of a wound."

As Applicant discussed previously, the Poelstra et al. reference teaches that alkaline phosphatase has endotoxin-detoxifying activity and therefore, can be used systemically to treat or prevent the complications due to infections with Gram-negative bacteria (*e.g.*, sepsis). The Poelstra et al. reference teaches systemic administration of alkaline phosphatase (see, for example, column 7, lines 45-47; column 11, lines 22-23; and column 13, line 63 -- column 14, line 3). The paragraph at column 4 teaches that those alkaline phosphatases that cannot be systemically administered can be "immobilized in situ at the location of a wound." In the context of the Poelstra et al. reference, "in situ at the location of a wound" refers to contacting the bone at the site of a wound. The Poelstra et al. reference does not teach or suggest that placental alkaline phosphatase can be formulated for topical delivery as is recited in claim 1. In addition, the Poelstra et al. reference does not teach or suggest that placental alkaline phosphatase can stimulate proliferation of fibroblasts.

With respect to the Millan et al. reference, the Examiner specifically referred to pages 2 and 3 in the telephone conference of February 12, 2004, to support the obviousness rejection. The Millan et al. reference is a review article on the biology of alkaline phosphatases. Pages 2 and 3 of the Millan et al. reference generally discuss the gene structure of different types of alkaline phosphatases including placental alkaline phosphatase. The Millan et al. reference teaches that developmentally, placental alkaline phosphatase plays a role in feto-maternal

metabolism and placental differentiation (see, for example, pages 17 and 19-21). The Millan et al. reference does not teach or suggest that placental alkaline phosphatase can stimulate proliferation of fibroblasts.

Even in combination, the Poelstra et al. reference and the Millan et al. reference do not suggest that placental alkaline phosphatase can stimulate proliferation of fibroblasts. The Millan et al. reference teaches that tissue non-specific alkaline phosphatases (TNAPs) are involved in bone mineralization (see page 18), which suggests that the alkaline phosphatase referred to in column 4 of the Poelstra et al. reference for improving bone mineralization may be a TNAP.

Applicants submit that this is a clear case of hindsight in which the Examiner has combined references that utilize a gel material in a wound healing composition (Sugitachi et al., Fischer et al., DE 3007226, and WO 92/14480) with references that describe alkaline phosphatases (Poelstra et al. and Millan et al.). According to *Interconnect Planning Corp. v. Feil* (744 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985)), "[i]t is [an] error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a 'blueprint.' When prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight obtained from the invention itself." As stated previously, none of the references, alone or in combination, teach or suggest using *placental* alkaline phosphatase formulated for *topical* delivery in an amount effective to *stimulate proliferation of fibroblasts* to treat *skin* wounds.

Although the cited references do not make obvious the claimed invention, Applicant also has presented evidence of unexpected results. The ability of placental alkaline phosphatase to stimulate production of skin fibroblasts is an unexpected result. "In the present approaches, contrary to earlier work, it has been discovered that PALP...stimulate[s] proliferation of adult fibroblasts, in particular adult skin fibroblasts." See the sentence bridging pages 5 and 6 of the specification.

In view of the remarks herein, Applicant respectfully requests that the rejection of claims 1, 4, 7-9, 27, and 31 under 35 U.S.C. §103(a) be withdrawn.

Request for Rejoinder

Claims 3, 5, 6, 10, 29, and 30 were withdrawn as directed to a non-elected species following the Restriction Requirement of November 5, 2002 and Applicant's election of December 5, 2002. Since claim 1 should be allowable in view of the remarks herein, Applicant respectfully requests that claims 3, 5, 6, 10, 29, and 30 be rejoined and allowed pursuant to MPEP §809.02(c)(B)(1).

Further, Applicant requests that the Examiner consider rejoining the claims directed to an article of manufacture containing the composition of claim 1 (essentially corresponding to cancelled claims 32-35). According to the TC1600 Restriction Practice Action Plan (a copy of which was enclosed with the November 21, 2003 Response After Final), the U.S. Patent and Trademark Office plans to publish claim sets that will be examined together regardless of whether they can otherwise be restricted under 35 U.S.C. §121 because the search and examination of the claims do not present a serious burden on the Office. Applicant submits that the claims directed toward articles of manufacture containing the composition recited in pending claim 1 are an example of claims that do not present an additional search burden on the Examiner. Applicant submits that these claims should be entitled to rejoinder. If the Examiner agrees, Applicant will add the article of manufacture claims by amendment.

CONCLUSIONS

Applicant asks that claims 1, 3, 4, 5, 6, 7-9, 10, and 29, 30, and 31 be allowed in view of the remarks herein. Please apply the amount of $850 ($375 for the RCE filing fee and $475 for the Petition for Extension of Time) to Deposit Account 06-1050.

Respectfully submitted,

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